#13

EXPRESS MAIL CERTIFICATE

OIPE JC12 APR 19 2002 PATENT & TRADEMARK OFFICE

Date 4-19-02 Label No. EV039137506US

I hereby certify that, on the date indicated above, this paper or fee was deposited with the U.S. Postal Service & that it was addressed for delivery to the Assistant Commissioner for Patents, Washington, DC 20231 by "Express Mail Post Office to Addressee" service.

PATRICIA A. RUBIO Patricia A. Rubio
Name (Print) Signature

PLEASE CHARGE ANY DEFICIENCY UP TO $300.00 OR CREDIT ANY EXCESS IN THE FEES DUE WITH THIS DOCUMENT TO OUR DEPOSIT ACCOUNT NO. 04 – 0100

07278
PATENT TRADEMARK OFFICE

File No. 5432/01004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ken Liljegren *et al.*

Serial No.: 09/730,380 Group Art Unit: 1625

Filed: December 5, 2000 Examiner: C. Aulakh

For: PHARMACEUTICAL COMPOSITION CONTAINING CITALOPRAM

DECLARATION UNDER 37 C.F.R. §1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Hans Petersen, Head of Department of Special Chemistry at H. Lundbeck A/S, Copenhagen-Valby, Denmark, hereby declare that:

1. I have a M.Sc. Degree conferred in 1987 in Experimental Biology with a Specialty in Organic Chemistry from Odense University in Denmark.

2. I have been employed as a chemist in the pharmaceutical industry since 1989. Since September 2000, I have been the Head of the Department of Special Chemistry of H. Lundbeck A/S. Since 1996 to the present, I have been actively involved in the development of processes of manufacturing Citalopram and crystallized salts of Citalopram. I am an inventor

on more than 20 International patent applications which have been filed covering methods of manufacturing Citalopram. Many of the International applications have entered prosecution in various national and regional patent offices, including the United States Patent and Trademark Office. A copy of my *curriculum vitae* is attached at **Exhibit 1.**

3. I have reviewed the specification and claims of the above-captioned U.S. patent application. I understand that claims 16-19, 44 and 45 (the product claims) cover crystals of a salt of Citalopram wherein the crystals have a median particle size of at least 40 μm, and that claims 20-33 and 46-58 (the method claims) cover methods of manufacturing a salt of Citalopram wherein the median particle size of the salt is at least 40 μm.

4. I understand that product claims and method claims have been rejected as anticipated by U.S. Patent Nos. 4,943,590 (the '590 patent) (**Exhibit 2**) and 4,136,193 (the '193 patent). I am familiar with the '590 and '193 patents. To the best of my knowledge, the method of manufacturing crystallized salts of Citalopram in the '590 patent necessarily results in crystals having a particle size of less than 40 μm. The '193 patent does not describe any methods of making crystallized salts of Citalopram.

5. I am also familiar with methods of synthesizing crystallized salts of Citalopram which were known before October 27, 2000. To the best of my knowledge, as of October 27, 2000, all known methods of manufacturing crystallized salts of Citalopram resulted in crystals having a median particle size of less than 40μm. To the best of my knowledge, the only methods of synthesizing Citalopram crystals known before October 27, 2000 were disclosed in Example 2 of U.S. Patent No. 4,650,884 (the '884 patent) (**Exhibit 3**), published March 17, 1987, and in Example 3 of the '590 patent, published July 24, 1990.

6. In February 2002, I was asked by patent attorneys of H. Lundbeck A/S to conduct crystallizations of citalopram hydrobromide according to the procedures described in the '884 and '590 patents, and to measure the median particle size of the resulting crystals. I planned and organized these crystallizations, which were completed on March 15, 2002 under my

supervision at the laboratories of H. Lundbeck A/S. The results of these tests are described in paragraphs 7-14 below.

7. Citalopram hydrobromide is produced at our production plant according to the procedure disclosed in Example 2 of the '884 patent (col. 5, l. 7 - col. 6, l. 5). A sample of crude citalopram base dissolved in toluene was taken from the production line at a point immediately after the silica gel filtration of Example 2 of the '884 patent (col. 5, l. 20). The sample was evaporated under a reduced pressure until a maximum temperature of 50°C was reached. The residue was dissolved in acetone, treated with charcoal and filtered, and the filtrate was cooled to 20°C. Gaseous hydrogen bromide was then introduced during 2 hours at 20-25°C until a pH of 3 was reached. The pH was then adjusted to 7 by adding some of the acetone solution of crude citalopram base. The mixture was left overnight to form crystals. The resulting crystals were filtered and washed with hexane and then acetone, and dried at 45°C. A sample (Sample 1) was taken for particle size analysis. The remaining crystals were then dissolved in water at about 55°C, treated with charcoal and filtered, cooled to 20°C and left overnight for crystallization, after addition of seed crystals. The resulting crystals were filtered, washed with water and dried. A sample (Sample 2) was taken for particle size analysis. The remaining crystals were then dissolved in a mixture of methanol and 2-propanol (1:2) at 70°C, treated with charcoal, filtered, cooled to 20°C and left overnight for crystallization. The resulting crystals were filtered, washed with a mixture of methanol and 2-propanol (1:2) and dried. A sample (Sample 3) was taken for particle size analysis. The remaining crystals were then dissolved in a mixture of methanol and acetone (1:4) at 55°C, treated with charcoal, filtered, and cooled to 20°C. After addition of seed crystals, hexane (8 times the amount of methanol) was added slowly during 1 hour and the mixture was left overnight for crystallization. The resulting crystals were filtered, washed with a mixture of acetone and hexane (1:2) and dried. A sample (Sample 4) was taken for particle size analysis.

8. According to the crystallization procedure disclosed in Example 3 of the '590 patent, citalopram base was dissolved in a 2:1 mixture of 2-propanol and methanol, and an equivalent amount of gaseous hydrogen bromide was added. The mixture was left overnight and

the precipitated hydrobromide was filtered off and dried. A sample (Sample 5) was taken for particle size analysis.

9. In the March 15, 2002 tests, Citalopram crystals were formed according to five experiments, and were identified as Samples 1-5. Samples 1-4 were the results of the crystallization method of the '884 patent, and Sample 5 was the result of the crystallization of the '590 patent. For each of samples 1-5, the crystals agglomerated during drying into lumps of up to 1 cm in diameter. These lumps were easily broken by a light grinding in a mortar for all samples except Sample 1. The median particle size was determined after the lumps were broken.

10. Table 1 below contains the results of the testing of median particle size for the crystals of Samples 1-5:

TABLE 1

Sample	Crystallization Method	Median Particle Size (μm)
1	'884 Patent, precipitation	6
2	'884 Patent, first crystallization	14.7
3	'884 Patent, second crystallization	6.8
4	'884 Patent, third crystallization	14.7
5	'590 Patent, precipitation	6.2

11. The results of the particle size distribution tests of Sample 1 are attached at **Exhibit** 4. The chart depicts a bimodal particle size distribution with a first mode around 6 μm, and a second mode of greater than 200 μm. The apparatus indicated that oversized particles were present. The apparatus used to measure particle size has a cut-off of 200 μm. The analysis was redone, whereby the particles were ground more thoroughly and sieved through a 300 μm screen before the particle size analysis. The result was similar to the first analysis and there were still oversized particles. The oversized particles resulted from the presence of impurities which were present in the crude Citalopram (from the mother liquor) used in the synthesis of crystals. The impurities deposited onto the crystals during drying and glued the crystals together in strong agglomerates. The resulting particle size distribution tests revealed a bimodal distribution, with a first mode of approximately 6 μm and a second mode above 200 μm. The distribution around 6 μm is the free Citalopram crystals, while the distribution above 200 μm results from the agglomeration.

12. The results of the particle size distribution tests of Sample 2 are attached at **Exhibit** 5. The chart depicts a median particle size of 14.7 μm. The results of the particle size distribution tests of Sample 3 are attached at **Exhibit** 6. The chart depicts a median particle size of 6.8 μm. The results of the particle size distribution of Sample 4 are attached at **Exhibit** 7. The chart depicts a median particle size of 14.7 μm. The test results support my statement that the prior art methods of manufacturing Citalopram disclosed in the '884 and '590 patents form crystals having a median particle size of less than 40 μm.

13. In contrast to the prior art methods, the method of the invention results in crystals of Citalopram having a particle size greater than 40 μm. I am familiar with the experiments described in Examples 1, 2 and 4 at pages 9-10 of the above-captioned application. These examples demonstrate that the crystallization method of the invention produces crystals having a median particle size of greater than 40 μm.

14. It is believed that the crystallization methods of the '590 and '193 patents form smaller crystals because they are rapid crystallizations which result in high degrees of supersaturation. The supersaturation causes high nucleation rates relative to the particle growth rate, which result in small crystals. Prior to the experiments which led to this patent application, there were no known methods to form Citalopram crystals by slower crystallizations than those described in the '590 and '193 patents.

15. In contrast to the prior art crystallizations, the crystallization method of the present application is a controlled, slower crystallization resulting in low degrees of supersaturation and low nucleation rates relative to the particle growth rate. This results in larger crystals than were formed by previous crystallization methods.

16. I further declare that all statements made herein are based on information and belief and are believed to be true and that these statements were made with the knowledge that willful false statements made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

Date 17.04.2002

Hans Petersen

::ODMA\WORLDOX\M:\5432\6\004\JCT5018.DOC

H. Lundbeck A/S

CURRICULUM VITAE

Name:	**HANS PETERSEN**	**Date of birth:**	**4. December 1960**
Position:	**Head of Department**	**Date of employment:**	**1 OCTOBER 1996**

EDUCATION:

Year	Education	Educational Institution
1987	Cand. scient. (MSc) in "Experimental Biology with speciality on Organic Chemistry", The Chemical Institute	Odense University

PROFESSIONAL EXPERIENCE:

Period — **Position / Company, department, country / Major responsibilities**

09/00 – Head of Department: Dept of Special Chemistry (309), H. Lundbeck A/S

- Process and pharmaceutical patents to protect Citalopram and Escitalopram. Strategy to control generic citalopram. Development of other strategic processes

10/96 – 09/00 Patent chemist, H. Lundbeck A/S

- Process and pharmaceutical patents to protect Citalopram and Escitalopram. Strategy to control generic citalopram.

1995-96 NOVO NORDISK A/S

Chemical Development

- Development of a tri- and pentapeptide in the NSAC-project

1994 ABBOTT LABS.

Chem. and Pharm. Dev., North Chicago, USA

- Synthesis of decomposition products in tiagabine tablets

1989-94 NOVO NORDISK A/S

Chemical Development

- Development of the synthesis to Tiagabine and other development projects

1987-89 Copenhagen University, H C Ørsted Institute

- Synthesis of Glycosphingolipids and new glycosidation methods. Supervisor: Prof. Dr. Ole Buchardt

1987 DAK A/S

- Hydrolytic decomposition compounds of Caffein

PROFESSIONAL EXPERIENCE:

Period	Position / Company, department, country / Major responsibilities
1987	GEA A/S
	• Process patent to Ranitidine

SUPPLEMENTARY EDUCATION/TRAINING :

Year	Activity	Organised by
2001	Cross Cutural Awareness, Ken Blanchard	H.Lundbeck
	LMPD Module 1	
2000	Biocatalysis. Workshop, Amsterdam	Sci Update
	Biocatalysis. Conference, Amsterdam	Sci. Update
	Ind. Synth. of Optically active Comp.	Sci Update, Boston
	Chiral USA	Sci. Update, Boston
1999	Oxidation in Org. Chem.	Southampton, UK
	Int. Conf. Org. Prod. R&D	Sci. Update, New Orleans
	Prog. Dev. Symp.	Cambrigde, UK
1998	Int. Conf. Org. Prod. R&D	Sci. Update, San Fransisco
	Synth. and Methods	Sci. Update, Cumbria, UK
1997	Office 97	H. Lundbeck A/S
	Prog. Dev. Symp,	Manchester, UK
1996	Regulatory Report writing	BIOS, DK
	Recent Org. Synth.	York, UK
	Belg. Org. Synth. Symp.	Gent. BEL
	Prog. Dev. Symp.	Manchester. UK
1995	Heterocyclic Chem.	Taipei, Taiwan
	Heterocyclic Chem.	Hong Kong
1994	GLP for Study Directors	Int. Health and Enrv. Edu., DK
	Johnson symp.	Stanford, USA
	MPPCC	Chicago, USA
1993	Hydride Symp.	Chemetall AG, Goslar, GER
	Eur. Organic Chem.	Barcelona, ESP
	GMP	Novo Nordisk A/S
	"Fra ide til salg" / From Idea to sale	Novo Nordisk A/S
1992	Chem. Dev. and Scale Up	Novo Nordisk A/S
	GMP on SOP	Novo Nordisk A/S
1991	Heterocyclic Chem.	IUPAC, Corvallis, Oregon, USA
1990	Pre-Clinical dev., Oxford Workshops	
	GMP	Novo Nordisk A/S
	Chirality in Drug Design	SKF, Cambrigde, UK
1989	Patentkursus (P&V), Patent course	

MEMBERSHIP OF PROFESSIONAL SOCIETIES :

Member of
- Kemisk Forening, Copenhagen
- ACS, Washington D.C.
- SCI, London

PUBLICATIONS AND PRESENTATIONS :

2001

- Andersen, Knud Erik; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Huusfeldt, Per O.; Suzdak, Peter D.; Swedberg, Michael D. B.: **Synthesis of novel GABA uptake inhibitors. Part 6: Preparation and evaluation of N-Ω asymmetrically substituted nipecotic acid derivates**. Health Care Dicovery, Novo Nordisk A/S, Malov, Den. Biorg. Med. Chem. (2001), 9(11), 2773-2785
- Petersen, Hans; Dancer, Robert: **Preparation of citalopram.** PCT Int. Appl. (2001). *WO 0185712*
- Petersen, Hans: **Preparation of 5-cyano-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran**. PCT Int. Appl. (2001). *WO 0168632*
- Petersen, Hans: **Method for the preparation of citalopram** . PCT Int. Appl. (2001). *WO 0168631*
- Petersen, Hans: **Method for the preparation of citalopram** . PCT Int. Appl. (2001). *WO 0168630*
- Petersen, Hans; Ahmadian, Haleh: **Stepwise alkylation of 5-substituted 1-(4-fluorophenyl)-1,3-dihydroisobenzofurans (citalopram intermediates)**. PCT Int. Appl. (2001). *WO 0168629*
- Petersen, Hans: **Method for the preparation of citalopram** . PCT Int. Appl. (2001). *WO 0168628*
- Petersen, Hans; Rock, Michael Harold: **Method for the preparation of citalopram**. Brit. UK Pat. Appl. (2001). *GB 2354240*
- Petersen, Hans: **Method for the Preparation of 5-cyanophthalide from oxaline- or thiazoline-substituted derivs.** PCT Int. Appl. (2001) *WO 0151477*
- Petersen, Hans; Rock, Michael: **Cyanidation method and the catalysts for the preparation of the 5-cyanophthalide citalopram intermediate**. PCT Int. Appl. (2001). *WO 0149672*
- Petersen, Hans; Felding, Jacob: **Method for the preparation of citalopram** . PCTInt. Appl. (2001). *WO 0147909*
- Petersen, Hans; Rock, Michael Harold: **Method for the preparation of citalopram by nickel-catalyzed cyanation of halo precursors.** Brit. UK Pat. Appl. (2001). *GB 2354240*
- Andersen, Knud Erik; Sorensen, Jan L.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Huusfeldt, Per O.; Suzdak, Peter D.; Swedberg, Michael, D. B.: **Synthesis of Novel γ-Aminobutyric Acid (GABA) Uptake Inhibitors. %. Preparation and structure -Activity Studies of Tricyclic Analogues of Known GABA Uptake Inhibitors.** Health Care Discovery, Novo Nordisk A/S, Malov, Den. J. Med. Chem. (2001), 44(13), 2152-2163.
- Petersen, Hans: **Method for the preparation of 5-carboxyphtalide from terephthalidc acid and trioxane or paraformaldehyde**. PCT Int. Appl. (2001). *WO 0132643*
- Petersen, Hans; Dahlberg Nielsen, Poul: **Method for the preparation of 5-carboxyphtalide**. PCT Int. Appl. (2001). *WO 0132642*

2000

- Petersen, Hans; Dahlberg Nielsen, Poul: **Esterification, amidation and dehydration method for the preparation of 5-cyanophtalide**. PCT Int. Appl. (2000). *WO 0039112*
- Dall'asta, Leone; Casazza, Umberto; Petersen, Hans: **Method for the preparation of citalopram.** PCT Int. Appl. (2000). *WO 0023431*

PUBLICATIONS AND PRESENTATIONS :

- Petersen, Hans; Rock, Michael Harold; Svane, Henrik: **Method for the preparation of citalopram**. PCT Int. Appl. (2000). *WO 0013648*
- Rock, Michael Harold; Petersen, Hans; Ellegaard, Peter: **Method for the preparation of citalopram**. PCT int. Appl. (2000). *WO 0012044*

1999

- Andersen, Knud Erik; Sorensen, Jan L.; Huusfeldt, Per O.; Knutsen, Lars J. S.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Suzdak, Peter D.; Swedberg, Michael D. B.: **Synthesis of Novel GABA Uptake Inhibitors. 4. Bioisosteric Transformation and Successive Optimization of Known GABA Uptake Inhibitors Leading to a Series of Potent Anticonvulsant Drug Candidates**. J. Med. Chem (1999) 42(21)
- Peschke, Bernd; Ankersen, Michael, Hansen, Birgitte Sehested; Hansen, Thomas Kruse; Johansen, Nils Langeland; Lau, Jesper; Madsen, Kjeld; Petersen, Hans; Thogersen, Henning; Watson, Brett.: **Synthesis and in vitro characterization of new growth hormone secretagogues derived from ipamorelin with dipeptidomimetic N-terminals**. Eur. J. Med. Chem (1999), 34(5), 363-380
- Knutsen, Lars J. S.; Lau, Jesper; Petersen, Hans; Thomsen, Christian; Weis, Jan U.; Shalmi, Michael; Judge, Martin E.; Hansen, Anker Jon; Sheardown, Malcolm J.: **N-substituted Adenosines as Novel Neuroprotective A1 Agonists with Diminished Hypotensive Effects**. J. Med. Chem. (1999), 42(18), 3463-3477
- Knutsen, Lars J.S.; Andersen, Knud Erik; Lau, Jesper; Lundt, Behrend F.; Henry Rodger F.; Morton, Howard E.; Nrum, Lars; Petersen, Hans, Stephensen, Henrik; Suzdak, Peter D; Swedberg, Michael D. B.; Thomsen, Christian; Sorensen, Per O.: **Synthesis of Novel GABA Uptake Inhibitors. 3. Diaryloxime and Diarylvinyl Ether Derivatives of Nipecotic Acid and Guvacine as Anticonvulsant Agents**. J. Med. Chem. (1999), 42(18), 3447-3462
- Petersen, Hans: **Method for the preparation of Citalopram**. PCT Int. Appl. (1999) 18 pp. *WO 9930548*

1998

- Petersen, Hans; Bregnedal, Peter; Bogeso, Klaus Peter: **Method for the preparation of citalopram**. PCT Int. Appl. (1998), 17 pp. *WO 9819513*
- Petersen, Hans; Bregnedal, Peter; Bogeso, Klaus Peter: **Method for the preparation of citalopram**. PCT Int. Appl. (1998) 14 pp. *WO 9819512*
- Petersen, Hans; Bogeso, Klaus Peter; Bech Sommer, Michael; **Method for the preparation of citalopram**. PCT Int. Appl.. (1998) 16 pp. *WO 9819511*

1996

- Andersen, Henrik Sune; Andersen, Knud Erik; Madsen, Peter; Joergensen, Tine Krogh; Hohlweg, Rolf; Petersen, Hans; Olsen, Uffe Bang **Preparation of N-heterocyclylalkyl-substituted 3-pyridinecarboxylic acids and esters for treatment of neurogenic inflammation and insulin resisteance in NIDDM or aging**. PCT Int. Appl. (1996), 55 pp. *WO 9631469*
- Chorghade, M.S.; Petersen, H.; Lee, E. C.; Bain, S. **Efficient syntheses of regioisomers of tiagabine**. Pure Appl. Chem. (1996), 68(3), 761-763
- Andersen, Knud E.; Begstrup, Mikael; Chorghade, Mukund S.; Lee, Elaine C.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Sqerensen, Per O.; Thoegersen, Henning: **The synthesis of novel Gaba uptake inhibitors. II. Synthesis of 5-hydroxytiagabine, a human metabolite of the GABA reuptake inhibitor tiagabine. [Erratum to document cited in CA121:205185].** Tetrahedron (1996), 52(19), 3375

1995

- Andersen, Knud Erik; Olsen, Uffe Bang; Petersen, Hans; Groenvald, Frederik Christian; Sonnewald, Ursula; Joergensen, Tine Krogh; Andersen, Henrik Sune: **Novel azaheterocyclic acids useful as analgetics and antiinflammatories**. PCT Int. Appl. (1995), 54 pp. *WO 9518793*

PUBLICATIONS AND PRESENTATIONS :

- Lau, Jesper; Petersen, Hans; Andersen, Knud Erik; Soerensen, Per Olaf; Lundt, Behrend Friedrich: **Preparation of 1-[(aralkoxy)alkyl]piperidine-3-carboxylates and analogs as GABA uptake inhibitors.** PCT Int. Appl. (1995), 41 pp. *WO 9500486*
- Petersen, Hans; Andersen, Knud Erik; Soerensen, Per Olaf; Lau, Jesper; Petersen, Henning Boerge; Lundt, Behrend Friedrich: **Preparation of N-(alkylideneaminooxyalkyl)piperidinecarboxylic acids and esters and their inhibition of GABA uptake.** PCT Int. Appl. (1995), 44 pp. *WO 9500483*
- Andersen, Knud Erik; Lau, Jesper; Soerensen, Per Olaf; Petersen, Hans; Lundt, Friedrich Behrend: **Preparation of 1-[(cycloalkylideneimino)oxyalkyl]-3-piperidinecarboxylates as GABA uptake inhibitors.** PCT Int Appl. (1995) 20 pp. *WO 9500484*
- Soerensen, Per Olaf; Lau, Jesper; Andersen, Knud Erik; Petersen, Hans; Lundt, Behrend Fredrich: **Preparation of 1-(aryloxyalkyl)piperidine-3-carboxylates as GABA uptake inhibitors.** PCT Int. Appl. (1995) 21 pp. *WO 9500485*

1994
- Callen, Gary; Chorghade, Mukund S.; Lee, Elaine C.; Nielsen, Peter G.; Petersen, Hans; Rustum, Abu: **Identification and synthesis of major oxidative degradation products of tiagabine.** Heterocycles (1994), 39(1), 293-303
- Andersen, Knud E.; Begstrup, Mikael; Chorghade, Mukund S.; Lee, Elaine C.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Soerensen, Per O.; Thoegersen, Hening: **The synthesis of novel GABA uptake inhibitors. Part 2. Synthesis of 5-hydroxytiagabine, a human metabolite of the GABA reuptake inhibitor tiagabine.** Tetrahydron (1994), 50(29), 8699-10
- Chorghade, Mukund S.; Ellegaard, Peter; Lee, Elaine C.; Petersen, Hans; Soerensen, Per Olaf: **Synthesis of desmethyl tiagabine.** Heterocycles (1994), 37(2), 783-92

1992
- Andersen, Knud Erik; Knutsen, Lars Jacob Stray; Soerensen, Per Olav; Lundt, Behrend Friedrich; Lau, Jesper; Petersen, hans: **Novel heterocyclic carboxylic acids.** PCT Int. Appl. (1992), 58 pp
- Hjuler-Nielsen, Hans Peter; Ped(t)ersen, Hans; Hansen, Henning Bue; Pedersen, Erik B.; Nielsen, Claus: **Synthesis of 3-(6-alkylaminopurin-9-yl)-2,3-dideoxy-D-threo-pentopyronoses and their reduction to 3-(6-alkylaminopurin-9-yl)-2,3-dideoxy-D-pentitols.** J. Heterocycl. Chem. (1992), 29(2), 511-13

1991
- Alhede, Boerge; Buchardt, Ole; Clausen, Finn Priess; MacCluskey, Klaus K.; Petersen, Hans: **Preparation of (N, N-dimethylaminomethyl)aryl compounds, e.g. ranitidine hydrochloride.** Ger. Offen. (1991), 9 pp.

1989
- Petersen, Hans; Pedersen, Erik B.; Nielsen, Carsten M: **Synthesis of 2,3-dideoxy-3-guaninyl-D-pentoses with potential antiviral activity.** Chem. Scr. (1989), 29(4), 375-8

1988
- Petersen, Hans; Motawia, Mohammed S.; Andreassen, Erik S.; Jacobsen, Jens Peter; Pedersen, Erik B.: **New routes to 2,3-dideoxy-3-phthalimido-D-hexoses.** Chem. Scr. (1988), 28(3), 341-5

*) **Incl. references to SciFinder**

Date and signature (employee):

Name:	HANS PETERSEN	Date of birth:	4. December 1960
Position:	Head of Department	Date of employment:	1 OCTOBER 1996

EDUCATION:

Year	Education	Educational Institution
1987	Cand. scient. (MSc) in "Experimental Biology with speciallity on Organic Chemistry", The Chemical Institute	Odense University

PROFESSIONAL EXPERIENCE:

Period — **Position / Company, department, country / Major responsibilities**

09/00 – Head of Department: Dept of Special Chemistry (309), H. Lundbeck A/S

- Process and pharmaceutical patents to protect Citalopram and Escitalopram. Strategy to control generic citalopram. Development of other strategic processes

10/96 – 09/00 Patent chemist, H. Lundbeck A/S

- Process and pharmaceutical patents to protect Citalopram and Escitalopram. Strategy to control generic citalopram.

1995-96 NOVO NORDISK A/S
Chemical Development

- Development of a tri- and pentapeptide in the NSAC-project

1994 ABBOTT LABS.
Chem. and Pharm. Dev., North Chicago, USA

- Synthesis of decomposition products in tiagabine tablets

1989-94 NOVO NORDISK A/S
Chemical Development

- Development of the synthesis to Tiagabine and other development projects

1987-89 Copenhagen University, H C Ørsted Institute

- Synthesis of Glycosphingolipids and new glycosidation methods. Supervisor: Prof. Dr. Ole Buchardt

1987 DAK A/S

- Hydrolytic decomposition compounds of Caffein

1987 GEA A/S

- Process patent to Ranitidine

PUBLICATIONS AND PRESENTATIONS :

2001-1988

- 43 publications, including 26 patents covering Citalopram.

15-mar-2002
CNO

Sympatec GmbH
System-Partikel-Technik

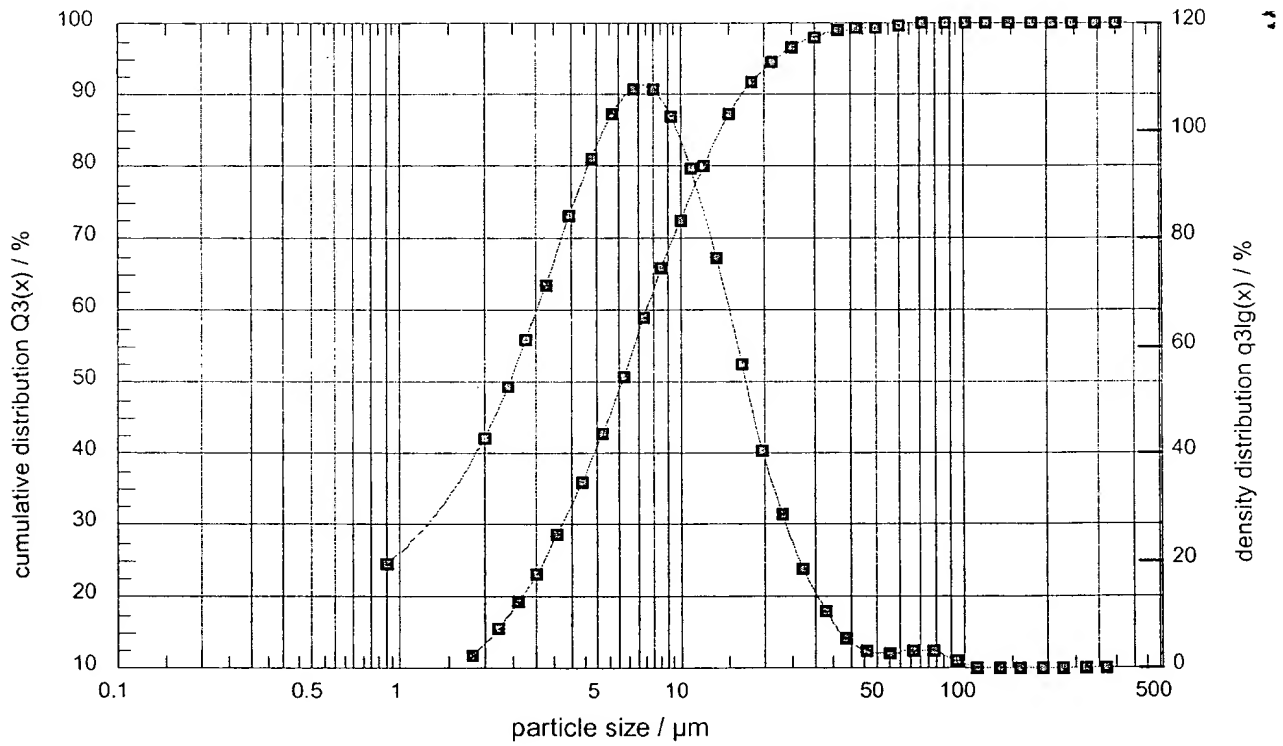
HELOS Particle Size Analysis

WINDOX

Sympatec HELOS (H0793) RODOS: Citalopram HBr 15-03-02 / 13:44:22

feeder:	VIBRI		Measuring conditions:	10s2.00%COptny	
pressure:	0,81	bar	measuring range:	R4: 0.5/1.8...350µm	
vacuum:	54,00	mbar	measuring duration:	10,01	s
feed rate:	100,00	%	cycle time:	1000	ms
funnel gap:	2,50	mm	start when:	2,00% at	button
revolution:	0,00	%	reference measurement:	00:00:32 , 0,00 %	
			evaluation:	HRLD (V 3.2 Rel.4)	

operator : CNO
identifier : 404/157.1_001
Comments:



Volume Size Distribution

x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%
1,80	11,49	7,40	58,68	30,00	97,86	122,00	100,00
2,20	15,21	8,60	65,68	36,00	98,69	146,00	100,00
2,60	18,99	10,00	72,38	42,00	99,04	174,00	100,00
3,00	22,78	12,00	79,71	50,00	99,26	206,00	100,00
3,60	28,41	15,00	87,10	60,00	99,46	246,00	100,00
4,40	35,72	18,00	91,56	72,00	99,70	294,00	100,00
5,20	42,58	21,00	94,27	86,00	99,92	350,00	100,00
6,20	50,42	25,00	96,41	102,00	100,00		

x5 =	1,07 µm	x50 =	6,15 µm	x95 =	22,37 µm
x10 =	1,63 µm	x90 =	16,95 µm	x99 =	41,30 µm
VMD =	8,39 µm	Sv =	1,54 m2/cm3	c_opt=	14,16 %

15-mar-2002 CNO

Sympatec GmbH
System-Partikel-Technik

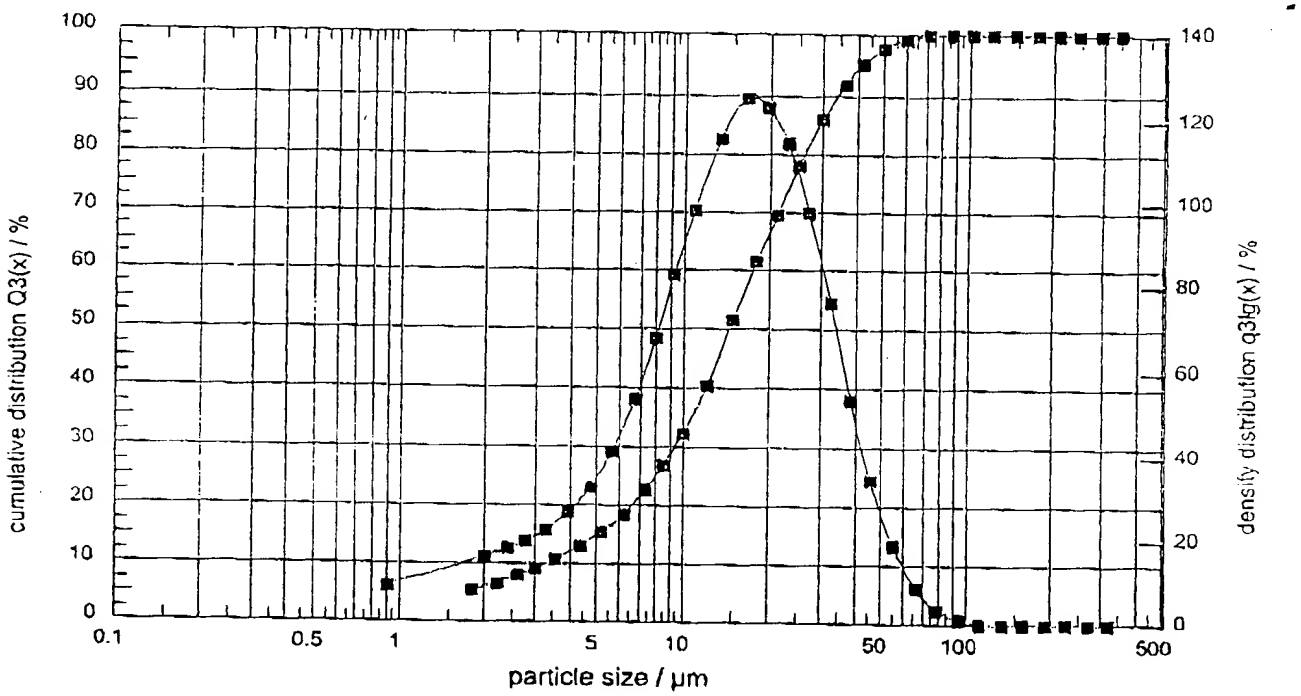
HELOS Particle Size Analysis

WINDOX

Sympatec HELOS (H0793) RODOS: Citalopram HBr 15-03-02 / 12:33:30

feeder:	VIBRI		Measuring conditions:	10s2.00%COptny	
pressure:	0,80	bar	measuring range:	R4: 0.5/1.8...350µm	
vacuum:	54,00	mbar	measuring duration:	10,01	s
feed rate:	100,00	%	cycle time:	1000	ms
funnel gap:	2,00	mm	start when:	2,00% at	button
revolution:	0,00	%	reference measurement:	00:00:43 , 0,00 %	
			evaluation:	HRLD (V 3.2 Rel.4)	

operator : CNO
identifier : 404/153b_001
Comments: Rflct 15-mar-2002 CNO



Volume Size Distribution

x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%
1,80	5,14	7,40	22,35	30,00	85,47	122,00	100,00
2,20	6,48	8,60	26,75	36,00	91,46	146,00	100,00
2,60	7,73	10,00	32,13	42,00	94,99	174,00	100,00
3,00	8,91	12,00	39,90	50,00	97,56	206,00	100,00
3,60	10,62	15,00	51,07	60,00	99,03	246,00	100,00
4,40	12,87	18,00	60,92	72,00	99,70	294,00	100,00
5,20	15,20	21,00	69,13	86,00	99,94	350,00	100,00
6,20	18,29	25,00	77,75	102,00	100,00		

x5 =	1,77 µm	x50 =	14,71 µm	x95 =	42,02 µm
x10 =	3,38 µm	x90 =	34,54 µm	x99 =	59,81 µm
VMD =	17,4 µm	Sv =	0,809 m2/cm3	c_opt=	4,80 %

15-mai-2002 CNO

Sympatec GmbH
System-Partikel-Technik

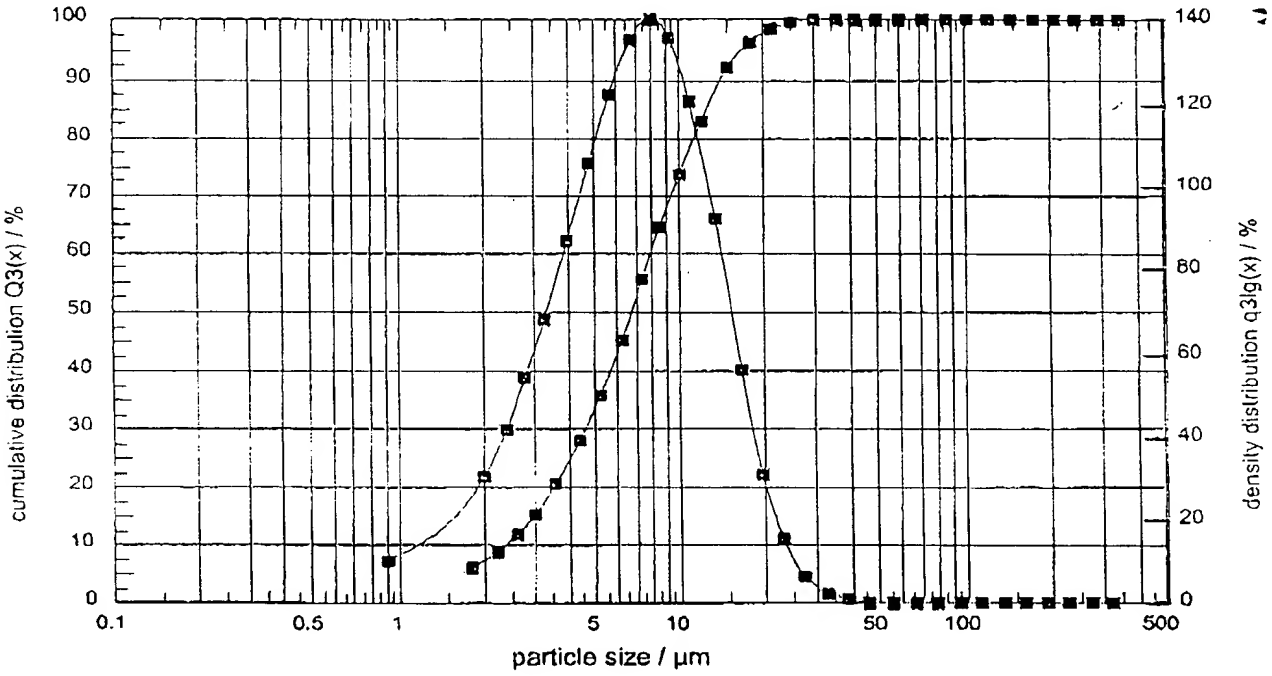
HELOS Particle Size Analysis

WINDOX

Sympatec HELOS (H0793) RODOS: Citalopram HBr 15-03-02 / 14:18:39

feeder:	VIBRI		Measuring conditions:	10s2.00%COptny	
pressure:	0,79	bar	measuring range:	R4: 0.5/1.8...350µm	
vacuum:	52,00	mbar	measuring duration:	10,01	s
feed rate:	100,00	%	cycle time:	1000	ms
funnel gap:	2,20	mm	start when:	2,00% at	button
revolution:	0,00	%	reference measurement:	00:00:50 , 0,00 %	
			evaluation:	HRLD (V 3.2 Rel.4)	

operator : CNO
identifier : 404/167.4_001
Comments: Mortet



Volume Size Distribution

x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%
1,80	5,99	7,40	55,21	30,00	99,81	122,00	100,00
2,20	8,63	8,60	64,34	36,00	99,96	146,00	100,00
2,60	11,66	10,00	73,21	42,00	100,00	174,00	100,00
3,00	14,99	12,00	82,76	50,00	100,00	206,00	100,00
3,60	20,36	15,00	91,66	60,00	100,00	246,00	100,00
4,40	27,89	18,00	96,10	72,00	100,00	294,00	100,00
5,20	35,53	21,00	98,16	86,00	100,00	350,00	100,00
6,20	44,84	25,00	99,32	102,00	100,00		

x5 =	1,59 µm	x50 =	6,80 µm	x95 =	17,26 µm
x10 =	2,38 µm	x90 =	14,44 µm	x99 =	23,89 µm
VMD =	7,78 µm	Sv =	1,28 m2/cm3	c_opt=	7,08 %

15-mar-2002 CNO

Sympatec GmbH
System-Partikel-Technik

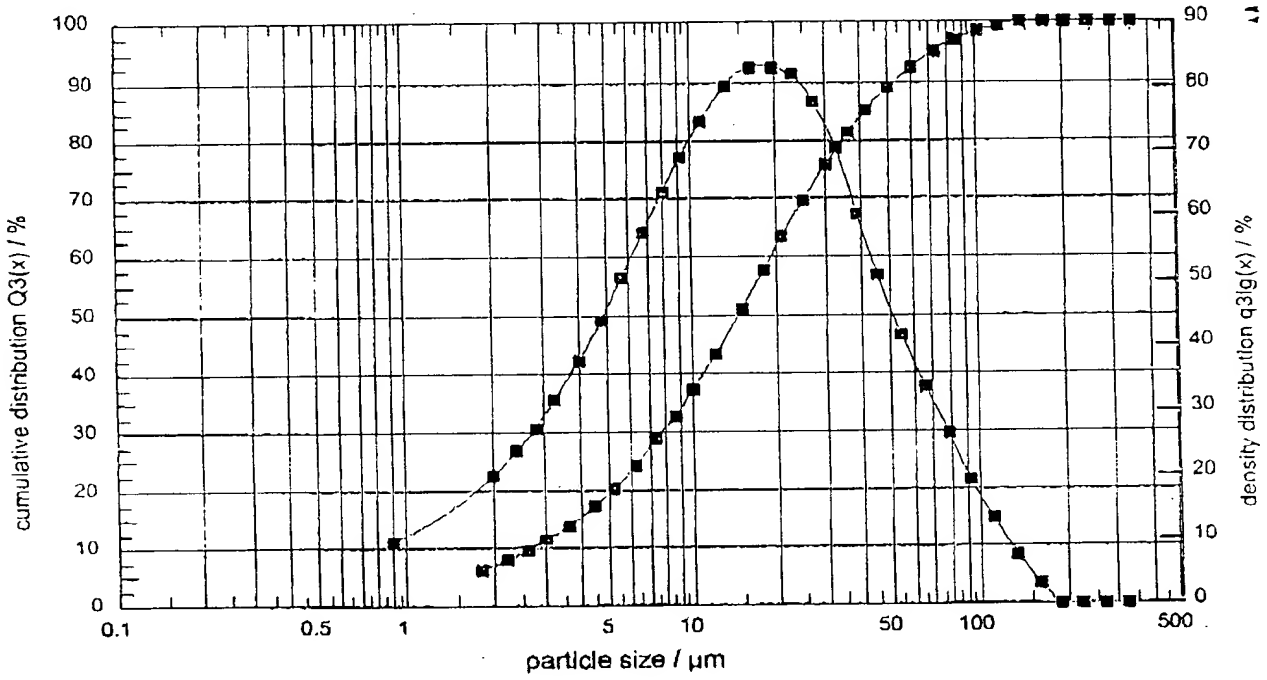
HELOS Particle Size Analysis

WINDOX

Sympatec HELOS (H0793) RODOS: Citalopram HBr 15-03-02 / 14:08:26

feeder:	VIBRI		Measuring conditions:	10s2.00%COptny
pressure:	0,80	bar	measuring range:	R4: 0.5/1.8...350µm
vacuum:	54,00	mbar	measuring duration:	7,00 s
feed rate:	100,00	%	cycle time:	1000 ms
funnel gap:	2,20	mm	start when:	2,00% at button
revolution:	0,00	%	reference measurement:	00:00:19 , 0,00 %
			evaluation:	HRLD (V 3.2 Rel.4)

operator : CNO
identifier : 404/167.3_001
Comments: Mortet



Volume Size Distribution

x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%
1,80	5,93	7,40	28,40	30,00	75,28	122,00	99,18
2,20	7,68	8,60	32,56	36,00	80,86	146,00	99,77
2,60	9,42	10,00	37,10	42,00	84,90	174,00	100,00
3,00	11,13	12,00	43,02	50,00	88,73	206,00	100,00
3,60	13,66	15,00	50,79	60,00	92,04	246,00	100,00
4,40	16,95	18,00	57,37	72,00	94,71	294,00	100,00
5,20	20,15	21,00	62,93	86,00	96,75	350,00	100,00
6,20	24,00	25,00	69,12	102,00	98,16		

x5 =	1,60 µm	x50 =	14,69 µm	x95 =	73,99 µm
x10 =	2,74 µm	x90 =	53,83 µm	x99 =	118,49 µm
VMD =	22,8 µm	Sv =	0,885 m2/cm3	c_opt=	17,79 %

15-mai-2002 CNO

Sympatec GmbH
System-Partikel-Technik

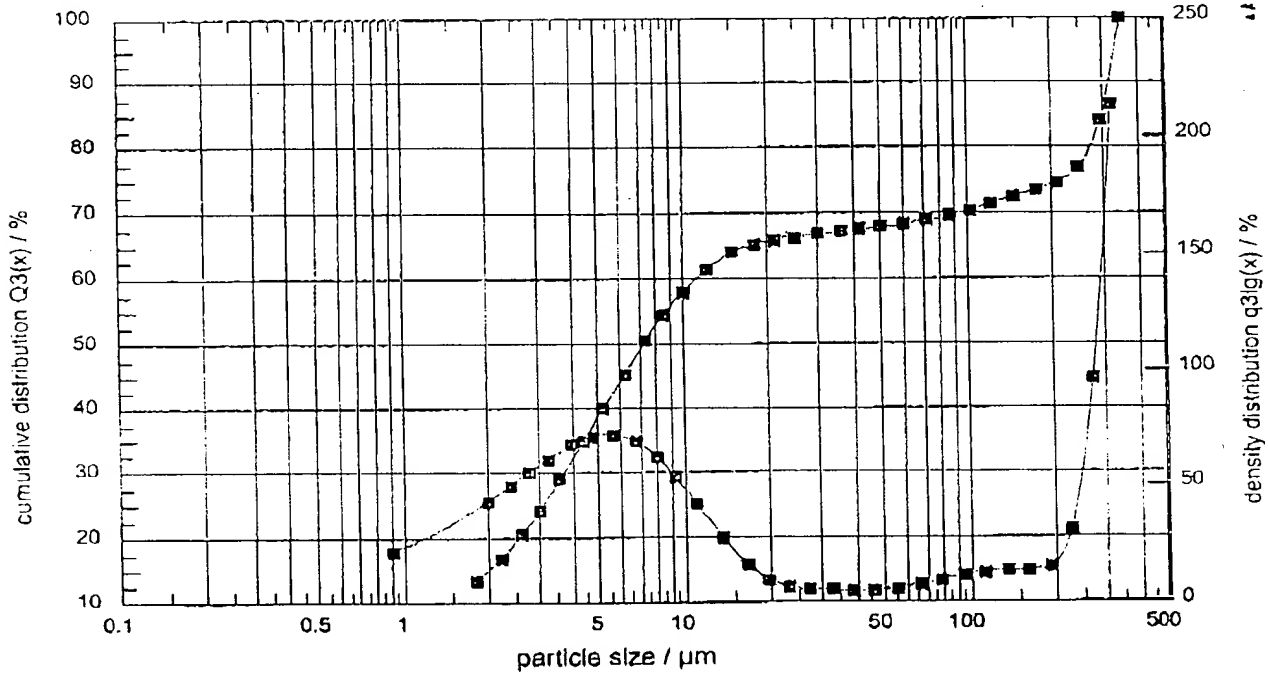
HELOS Particle Size Analysis

WINDOX

Sympatec HELOS (H0793) RODOS: Citalopram HBr 15-03-02 / 14:00:06

feeder:	VIBRI		Measuring conditions:	10s2.00%COptny
pressure:	0,79	bar	measuring range:	R4: 0.5/1.8...350µm
vacuum:	53,00	mbar	measuring duration:	10,01 s
feed rate:	100,00	%	cycle time:	1000 ms
funnel gap:	2,20	mm	start when:	2,00% at button
revolution:	0,00	%	reference measurement:	00:00:24 , 0,00 %
			evaluation:	HRLD (V 3.2 Rel.4)

operator : CNO
identifier : 404/167.2_001
Comments: ### Warning ### HRLD: Coarse particles probably exeeding measuring range
Mortet



Volume Size Distribution

x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%	x0/µm	Q3/%
1,80	13,11	7,40	50,41	30,00	66,60	122,00	71,13
2,20	16,86	8,60	54,43	36,00	66,98	146,00	72,16
2,60	20,46	10,00	57,89	42,00	67,29	174,00	73,15
3,00	23,90	12,00	61,18	50,00	67,64	206,00	74,23
3,60	28,73	15,00	63,87	60,00	68,09	246,00	76,58
4,40	34,58	18,00	65,10	72,00	68,67	294,00	83,97
5,20	39,72	21,00	65,70	86,00	69,37	350,00	100,00
6,20	45,16	25,00	66,18	102,00	70,17		

x5 =	1,00 µm	x50 =	7,31 µm	x95 =	332,53 µm
x10 =	1,49 µm	x90 =	315,07 µm	x99 =	346,51 µm
VMD =	88,9 µm	Sv =	1,41 m2/cm3	c_opt=	22,18 %